REMARKS

The Office Action dated June 18, 2002 presents the examination of claims 1-8, 12-14, and 25. Claims 1, 3, 5, 7, and 13 are canceled. Claims 2, 4, 6, 8-12, 14-16, 20, and 25 are amended. No new matter is inserted into the application.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 1-8, 12-14, and 25 under 35 U.S.C. § 112, second paragraph for allegedly being indefinite. Claims 1, 3, 5, 7, and 13 are canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection applied to the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Specifically, the Examiner asserts that the recitation of "tumor antigen peptide that is a partial peptide" is indefinite. The Examiner asserts that it is not clear whether the tumor antigen peptide comprises a sequence from another peptide. In order to answer this rejection, Applicants amend independent claim 2 to recite that the claimed tumor antigen peptide comprises an amino acid sequence that is a partial cyclophilin B sequence of SEQ ID NO: 44. No other claims recite "tumor antigen peptide that is a partial peptide."

Applicants respectfully submit that the metes and bounds of the claims are clearly set forth such that the requirements of 35

U.S.C. § 112, second paragraph are met. Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejects claims 1-8, 12-14, and 25 under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter not enabled by, nor described in, the specification. Claims 1, 3, 5, 7, and 13 are canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection applied to the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner argues that the claims encompass "any peptide" as long as it comprises a sequence in common with cyclophilin B, binds to HLA antigen, and is capable of being recognized by CTL.

Independent claim 2 is amended to recite that the claimed tumor antigen peptide comprises an amino acid sequence that is a partial cyclophilin B sequence of SEQ ID NO: 44. SEQ ID NO:44 shows the full-length amino acid sequence of cyclophilin B described in PNAS USA, 88L1903-1907 (1991) and of GenBank Accession No. M60857, as described on page 11, lines 16-18 of the specification. Therefore, the claims do not read on "any peptide."

The Examiner argues that the invention is further drawn to a derivative of a partial peptide derived from cyclophilin. Claims

2 and 4 are amended to no longer recite "a derivative thereof having the functionally equivalent properties…." Claim 6 is amended to limit derivatives to those in which the amino acid residue at position 2 and/or the C-terminus in the amino acid sequence shown in any one of SEQ ID NOs: 1-36 and 41-43 is substituted by another amino acid residue. Contrary to the Examiner's assertions, derivatives of the tumor antigen peptides are described, for example, on pages 17-22, Examples 8-10 of the specification. Therefore, there is adequate written description in the specification of derivatives of the claimed tumor antigen peptides, as recited in claim 6 and dependent claims therefrom. Furthermore, Applicants point out that the motifs necessary for the peptide to bind HLA is known, and are described, for example, on pages 12-13, Examples 4-7 of the specification. As such, it would not cause the skilled artisan to undue experimentation to make and use a derivative within the scope of claim 6.

The Examiner also specifically rejects claims 12-14 for lack of enablement. Specifically, the Examiner argues that there are no working examples or guidance showing that the tumor antigen peptides of the present invention may be used to treat or prevent tumors. In response to the Examiner's remarks, Applicants delete the term "pharmaceutical" and "for treating or preventing tumors" from claim 12. Claim 14 is amended into a method claim, directed to a method for treating or preventing tumors. Price (1991)

describes the cyclophilin B protein. However, no prior art describes or discloses that cyclophilin B acts as a tumor antigen protein, or has the activity to induce CTL. Thus, amended claim 14 is related to a new use of cyclophilin B as a tumor antigen protein.

For all of the above reasons, Applicants respectfully submit that the instant claims fully comply with 35 U.S.C. § 112, first paragraph. Withdrawal of the instant rejection is respectfully requested.

Rejection under 35 U.S.C. § 102

The Examiner rejects claims 1-8, 12-14, and 25 under 35 U.S.C. § 102(b) for allegedly being anticipated by Price (1991). Claims 1, 3, 5, 7, and 13 are canceled, thus rendering the rejection thereof moot. Applicants respectfully traverse the rejection applied to the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Price discloses the amino acid sequence of cyclophilin B. However, Price fails to disclose each and every limitation of the instant claims. Specifically, Price fails to disclose an isolated tumor antigen peptide that binds to an HLA antigen and is recognized by cytotoxic T lymphocytes.

As noted above, Price discloses the cyclophilin B protein. However, the entire sequence disclosed by Price not would bind to HLA antigen and be recognized by CTL. For example, only small peptides, i.e. peptides of between 8 and 15 amino acids, are capable of binding HLA antigen. This feature of peptides is described on page 13, line 3-4 of the specification. Therefore, the entire sequence as disclosed by Price would not bind HLA antigen and would not be recognized by CTL.

Further, Applicants submit a journal article (Boon, "Teaching the Immune System to Fight Cancer," *Scientific American*, March 1993) wherein the Figure on page 36 shows that only the tumor antigen **peptides** (depicted with the red bars indicated as PEPTIDES) bind to HLA antigen (depicted with the green indicated as CLASS I MHC), are presented on the cell surface, and are recognized by CTL (depicted with T LYMPHOCYTE). The Figure also shows that the tumor antigen **protein** (depicted with the red coil indicated as PROTEIN) does not undergo this process.

Accordingly, the claimed peptide comprising an amino acid sequence that is a partial cyclophilin B sequence is differentiated from the cyclophilin B protein. For these reasons, Price has not met every limitation of the claims and therefore fails to anticipate the claims. Withdrawal of the instant rejection is respectfully requested.

Sequence Listing

Enclosed herewith in full compliance to 37 C.F.R. §§1.821-1.825 is a substitute Sequence Listing to be inserted into the specification as indicated above. The substitute Sequence Listing in no way introduces new matter into the specification. Also submitted herewith in full compliance to 37 C.F.R. §§1.821-1.825 is a disk copy of the substitute Sequence Listing. The disk copy of the substitute Sequence Listing, file "2002-12-18 0020-4792P.ST25", is identical to the paper copy, except that it lacks formatting.

The enclosed substitute Sequence Listing is being filed in order to submit the sequence of SEQ ID NO: 44. SEQ ID NO:44 shows the full-length amino acid sequence of cyclophilin B described in PNAS USA, 88L1903-1907 (1991) and of GenBank Accession No. M60857, as described on page 11, lines 16-18 of the specification. No new matter is introduced by these amendments.

Conclusion

Applicants respectfully submit that the above amendments and/or remarks overcome the rejections of record. The instant claims recite patentable subject matter such that the present application is in condition for allowance. The Examiner is respectfully requested to issue a Notice of Allowability indicating that claims 2, 4, 6, 8-12, 14, and 25 are allowed.

If the Examiner has any questions concerning this application, the Examiner is requested to contact the Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at (703) 205-8000.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of three (3) months to December 16, 2002 in which to file a reply to the Office Action. The required fee of $920.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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JWB/KLR:gml/bsh

Attachment: Version with Markings to Show Changes Made
Boon, *Scientific American*, March 1993
Disk and paper copy of substitute Sequence Listing

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 1, 3, 5, 7, and 13 are canceled.

The following claims are amended:

Claim 2. (Amended) [A] An isolated tumor antigen peptide comprising an amino acid sequence that is a partial [peptide derived from] cyclophilin B sequence of SEQ ID NO:44, and that [is capable of binding] binds to an HLA antigen and [being] is recognized by cytotoxic T lymphocytes[, or a derivative thereof having the functionally equivalent properties].

Claim 4. (Amended) [The] An isolated tumor antigen peptide [of claim 3, that is selected from sequences comprising all or part of] comprising an amino acid sequence [shown in any one of] selected from the group consisting of SEQ ID NOs: 1-36 [or] and SEQ ID NOs: 41-43, [or a derivative thereof having the functionally equivalent properties] wherein the peptide binds to HLA antigen and is recognized by cytotoxic T lymphocytes.

Claim 6. (Amended) [The tumor antigen peptide derivative of claim 4, that is selected from sequences comprising all or part of an amino acid sequence] A derivative of the isolated tumor antigen peptide of claim 4, in which the amino acid residue

at position 2 and/or the C-terminus in the amino acid sequence [shown in any one of SEQ ID NOs: 1-36] is substituted by another amino acid residue, and in which the derivative binds to HLA antigen and is recognized by cytotoxic T lymphocytes.

Claim 8. (Amended) The [tumor antigen peptide] derivative of claim 6, [that is selected from sequences comprising all or part of an amino acid sequence] in which the amino acid residue at position 2 in the amino acid sequence shown in any one of SEQ ID NOs: 1-11 is substituted by tyrosine, phenylalanine, methionine, or tryptophan, and/or the amino acid residue at the C-terminus is substituted by phenylalanine, leucine, isoleucine, tryptophan, or methionine.

Claim 9. (Amended) The [tumor antigen peptide] derivative of claim 6, [that is selected from sequences comprising all or part of an amino acid sequence] in which the amino acid residue at position 2 in the amino acid sequence shown in any one of SEQ ID NOs: 12-36 is substituted by leucine, methionine, valine, isoleucine, or glutamine, and/or the amino acid residue at the C-terminus is substituted by valine or leucine.

Claim 10. (Amended) The [tumor antigen peptide] derivative of claim 8[, that is selected from sequences] comprising [all or part of] the amino acid sequence shown in SEQ ID NO: 37 or 38.

Claim 11. (Amended) The [tumor antigen peptide] derivative of claim 10[, that is selected from sequences] comprising [all or part of] the amino acid sequence shown in SEQ ID NO: 39 or 40.

Claim 12. (Twice Amended) A [pharmaceutical] composition [for treating or preventing tumors, that comprises] comprising as an active ingredient at least one of substances selected from tumor antigen peptides and derivates thereof according to any one of claims 2, 4, 6, 8, 10 or 11 [claim 1 or 2].

Claim 14. (Amended) A [pharmaceutical composition] method for treating or preventing tumors, [that] which comprises [as an active ingredient] administering a patient in need cyclophilin B, a partial polypeptide of cyclophilin B that comprises a tumor antigen peptide portion [capable of binding] which binds to an HLA antigen and [being] is recognized by cytotoxic T lymphocytes, or a gene encoding [the] cyclophilin B or [the] a partial polypeptide thereof.

Claim 15. (Twice Amended) An antibody that specifically binds to the tumor antigen peptide or the derivative thereof according to [claim 1 or 2] any one of claims 2, 4, or 6.

Claim 16. (Amended) An antigen-presenting cell wherein a complex between an HLA antigen and the tumor antigen peptide or the derivative thereof according to any one of claims [1-11] 2, 4, or 6 is presented on the surface of a cell having antigen-presenting ability that is isolated from a tumor patient.

Claim 20. (Twice Amended) A cytotoxic T lymphocyte that specifically recognizes a complex between an HLA antigen and a tumor antigen peptide or derivative thereof according to [claim 1 or 2] any one of claims 2, 4, or 6.

Claim 25. (Twice Amended) [A diagnostic agent for tumors that comprises as an active ingredient a tumor antigen peptide or a derivative thereof according to claim 1] The composition of claim 12 wherein the composition is to diagnose tumors.